UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,659	07/03/2001	Steven D. Tanksley	19603/3211 (CRF D-2594A)	2365

7590 08/06/2002

Michael L. Goldman, Esq.
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603-1051

EXAMINER	
BAUM, STUART F	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/898,659	Applicant(s) TANKSLEY, STEVEN D.	
	Examiner Stuart Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-55* is/are pending in the application.

4a) Of the above claim(s) *3 and 50-55* is/are withdrawn from consideration.

5)☒ Claim(s) *5,6,9 and 10* is/are allowed.

6)☒ Claim(s) *1,2,4,7,8 and 11-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-2, and 4-49 are drawn to isolated nucleic acid molecules of SEQ ID NO:1 and 3 encoding polypeptides of SEQ ID NO:2 and 4, an expression vector, a host cell transformed with said nucleic acid, a transgenic plant and plant seed, and methods for regulating fruit size and cell division, classified in class 800 subclass 290 for example.

II. Claim 3 is drawn to a *fw2.2* nucleic acid molecule, classified in class 536 subclass 23.1 for example.

III. Claims 50-55 are drawn to a protein classified in class 530 subclass 370 for example.

Inventions I, II, and III are unrelated to each other because nucleotide sequences either encoding different proteins or specifying specific expression patterns are structurally distinct chemical compounds and are unrelated to one another, as are different proteins structurally distinct chemical compounds and unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq (see MPEP 803.04 and 2434). This requirement is not to be construed as a requirement for an election of species, since each nucleotide and amino acid sequence is not a member of a single genus of invention, but constitutes an independent and patentably distinct invention.

Inventions I-III are distinct from each other because the starting materials, method steps and end products are distinct and unrelated to each other. Furthermore, the proteins of Invention III could be made by a process other than the expression of the gene of Inventions I and II, such as chemical synthesis or purification from the natural source, and the DNA of Invention I and II may be used for a process other than the production of a protein, such as a nucleic acid hybridization. Lastly, DNA and protein differ in composition, structure and function.

Each of Inventions I-III are capable of being separately made, independently used, and the patentability of one does not render the others obvious or unpatentable.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, fields of search, and classification, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Michael Goldman on 7/10/02 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-2, and 4-49 including SEQ ID NO:1 and 3 encoding SEQ ID NO:2 and 4, respectively. Affirmation of this election

must be made by applicant in replying to this Office action. Claims 3 and 50-55 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4, 7-8, and 11-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated nucleic acid molecule which encodes a protein that either regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule, or the nucleic acid molecule has a sequence of SEQ ID NO:1 or 3 encoding a protein of SEQ ID NO:2 or 4, or the nucleic acid molecule has a nucleic acid sequence that hybridizes to SEQ ID NO:1 or 3 under stringent conditions. The claims are also drawn to an expression vector comprising an above mentioned sequence, and host cell, transgenic plant, and transgenic plant seed comprising said vector, and including a method of regulating fruit size and cell division in plants comprising transforming a plant with said vector.

The Applicant claims any nucleic acid encoding any protein that regulates fruit size and/or cell division in plants but does not identify structural features unique to the hypothetic encoded protein, the functional domains of the protein nor the overall function of the protein. In addition, Applicant claims SEQ ID NO:1 and 3 but does not identify structural features unique to the encoded protein of SEQ ID NO:2 and 4, the functional domains of the protein nor the overall function of the protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Given the lack of description for the protein that regulates fruit size and/or cell division in plants, and the protein of SEQ ID NO:2 and 4, it remains unclear what features identify a protein that regulates fruit size and/or cell division in plants, and the protein of SEQ ID NO:2 and 4, including nucleic acid molecules encoding SEQ ID NO:2 and 4 that hybridize to SEQ ID NO:1 and 3 under stringent conditions. Since a protein that regulates fruit size and/or cell division in plants and the encoded proteins of SEQ ID NO:2 and have not been described by specific structural features or by specific function, the specification fails to provide an adequate written description to support the generic claims.

Claims 1-2, 4, 7-8, 11-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to an isolated *Lycopersicon pennellii*

ORFX gene of SEQ ID NO:1encoding SEQ ID NO:2 and an isolated *L. esculentum* ORFX gene of SEQ ID NO:3 encoding SEQ ID NO:4 and tomato transformation therewith, to obtain plants with smaller fruits as a result of less cell division does not reasonably provide enablement for claims broadly drawn to any isolated nucleic acid molecule encoding any protein that regulates fruit size or any plant nucleic acid molecule encoding any plant protein, or any sequence that hybridizes under stringent conditions characterized by a hybridization buffer comprising 0.9M sodium citrate buffer at a temperature of 45C or drawn to plant transformation with the exemplified or non-exemplified genes for obtaining a plant with increased or decreased fruit size and/or cell division. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to an isolated nucleic acid molecule which encodes a protein that either regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule, or the nucleic acid molecule has a sequence of SEQ ID NO:1 or 3 encoding a protein of SEQ ID NO:2 or 4, or the nucleic acid molecule has a nucleic acid sequence that hybridizes to SEQ ID NO:1 or 3 under stringent conditions. The claims are also drawn to an expression vector comprising an above mentioned sequence, and host cell, transgenic plant, and transgenic plant seed comprising said vector, and including methods of regulating fruit size and cell division in plants comprising transforming a plant with said vector.

The Applicants isolated their invention from *L. pennellii* and *L. esculentum* using the yeast artificial chromosome (YAC) containing the QTL *fw2.2* to screen cDNA libraries from the

respective tomato species. Once identified, the respective clones were sequenced and used to transform two tomato cultivars, Mogeor and TA496. The instant specification, however, fails to provide guidance for which amino acids of SEQ ID NO:2 and 4 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain activity of the encoded protein. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

It cannot be predicted by one of skill in the art that nucleic acids that hybridize to SEQ ID NO:1 or 3 under conditions as specified above will encode a protein with the same activity as SEQ ID NO:2 and 4. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine

residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Due to the unpredictable nature of plant transformation, one of skill in the art can not reasonably generate transformed plants with a desired phenotype using a specific isolated gene. Levels of transgene expression in plants are generally unpredictable and vary between independent transformants; this variability is usually explained by differences in transgene copy number and/or integration site (Finnegan and McElroy, 1994. Bio/technology 12: 883-888 pg. 883 2nd paragraph) Eshed et al (2001, Current Biology 11:1251-1260 pg 1255 2nd paragraph) documented the phenotypes of plants transformed with the 35S CaMV promoter fused to the *KANADI1* gene, which is a gene normally expressed in tissues located on the bottom side of young developing leaves. Of the 30 plants that were transformed with the *KANADI1* gene, 23 plants developed only small narrow cotyledons and an arrested meristem, three produced a few radialized leaves and four appeared normal. These results suggest that transforming plants with an endogenously expressed gene in regions of the plant in which it is not normally expressed produces highly unexpected and unpredictable results. For one skilled in the art, undue experimentation would be necessary to produce a plant with a desired phenotype while using an undefined enhancer region as a promoter.

Given the unpredictability of determining the function of an isolated nucleic acid other than SEQ ID NO:1 or 3 on the basis of its nucleotide sequence alone and the unpredictability of altering the phenotype of a plant by transforming it with an isolated nucleic acid that hybridizes

to SEQ ID NO:1 or 3, for the reasons stated above; given the lack of working examples of other genes other than SEQ ID NO:1 or 3; given the absence of guidance with regard to identification of other genes from the multitude of sequences that would hybridize to SEQ ID NO:1 or 3; and given the lack of working examples or guidance for isolating any nucleic acid molecule from any organism and from plants that encodes a protein that regulates fruit size and/or cell division in plants; given the state of the prior art which does not provide further guidance about other genes that can be used to regulate fruit size and/or cell division; and given the breadth of the claims which encompass a multitude of sequences that have not been exemplified, it would require undue experimentation by one skilled in the art to make and/or use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Bowman et al (1999, Development 126:2387-2396).

The claims are drawn to an isolated nucleic acid molecule, which encodes a protein that regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule.

Bowman et al teaches a *crc-1* mutant *Arabidopsis* plant exhibiting a reduced fruit size and the cloning of said mutant allele and as such anticipates the claimed invention.

Claims 1-2, 4, 8, 12-16, 18, 20, 22-23, 25, 27, 29, 30, 32, 34, 43-44, 46, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al (1998, WO 98/42851).

The claims are drawn to an isolated nucleic acid molecule which encodes a protein that either regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule. The claims are also drawn to an expression vector comprising an above-mentioned sequence, and host cell, transgenic plant, and transgenic plant seed comprising said vector, and including a method of regulating cell division including increasing and decreasing cell division in plants comprising transforming a plant with said vector.

Murray et al teach a plant DNA sequence that encodes a cell-division controlling protein (CYCD2 from *Arabidopsis*) that regulates cell division in plants. The DNA sequence is in a vector used to transform plants and would be passed on to the progeny seeds. Murray et al disclose a method of either increasing or decreasing cell division in plants by either over-expressing the *CYCD2* gene in sense orientation to increase cell division in plants which creates plants with larger organs compared to wild-type plants or expressing the *CYCD2* gene in antisense orientation which inhibits cell division in plants and thereby produces plants with smaller organs when compared to wild-type plants (page 29, line 24 and page 40, table 7). The above disclosure anticipates the claimed invention.

Claims 1-2, 8, 12-15, 17, 20, 22, 24, 27, 29, 31, 34, 36, 38, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Yanofsky et al (1999, WO 99/00503).

The claims are drawn to an isolated nucleic acid molecule which encodes a protein that either regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule. The claims are also drawn to an expression vector comprising an above-mentioned sequence, and host cell, transgenic plant, and transgenic plant seed comprising said vector, and including a method of regulating fruit size.

Yanofsky et al teach a plant DNA sequence (AGL8-related gene) that when over-expressed in *Arabidopsis* produces larger fruits compared to wild-type plants. The AGL8-related sequence would be in an expression vector, transformed into an *Arabidopsis* plant and would be passed on to the progeny seeds. Yanofsky et al teach a method of producing larger fruits comprising over-expressing the AGL8-related gene in *Arabidopsis*, (page 55, example II) and as such anticipate the claimed invention.

Claims 1-2, 4, 12-16, 18, 22-23, 25, 29-30, 32, 36-37, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Dai et al (1999, The Plant Cell 11:1253-1266).

The claims are drawn to an isolated nucleic acid molecule which encodes a protein that either regulates, increases or decreases fruit size and/or cell division in plants, wherein the nucleic acid molecule is a plant nucleic acid molecule. The claims are also drawn to an expression vector comprising an above-mentioned sequence, and host cell, transgenic plant, and transgenic plant seed comprising said vector, and including a method of regulating fruit size.

Dai et al teach a plant DNA sequence (AtHXK1) that when over-expressed in tomato produces smaller fruit. The AtHXK1 sequence would be in an expression vector, transformed tomato plants and would be passed on to the progeny seeds. Dai et al teach a method of

producing smaller fruits comprising over-expressing the ATHXK1 gene in tomato (page 1262, Figure 11) and as such anticipate the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 36, and 43 and all subsequent dependent claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, and 43 are indefinite in the recitation "regulates". This term is vague and does not set the metes and bounds of how fruit size and/or cell division is changed.

Claim 36 is indefinite in the recitation "under conditions effective to regulate fruit size". Applicant has not specified the conditions necessary to effectively regulate fruit size and as such this statement is open and ambiguous.

Claims 5-6, and 9-10 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:1 or 3 encoding SEQ ID NO:2 or 4.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 305-3015.

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1800

Stuart Baum Ph.D.

July 18, 2002